A DNA plasmid melanoma-targeting cancer vaccine, SCIB1, combined with either nivolumab and ipilimumab or pembrolizumab in pts with advanced unresectable melanoma: Efficacy and safety results from the open-label Phase 2 SCOPE trial.

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Background: Targeting of melanoma specific epitopes by T cells has been demonstrated to drive anti-tumour immune responses. SCIB1, is a novel DNA cancer vaccine incorporating CD8 and CD4 epitopes from TRP-2/gp100 into an antibody framework to allow Fc targeting of activated dendritic cells. SCIB1potentially has a synergistic effect on advanced unresectable melanoma when combined with checkpoint inhibitors (CPI) in the first-line setting improving the objective response rate.

Methods: Eligible pts with the target HLA type planned to be treated with standard of care CPI(s) were assigned to either cohort 1 (SCIB1 + nivolumab with ipilimumab) or cohort 2 (SCIB1 + pembrolizumab). SCIB1(8mg) was administered i.m. using a needle-free injection system at a fixed dosing schedule for a total of 10 doses over 24 months. The CPI therapy in cohorts 1 and 2 were administered i.v. in accordance with their respective SmPC. Safety was evaluated as a secondary endpoint in the main study. ORR as measured by RECIST 1.1 in the overall intention-to-treat population was the primary endpoint. The study is designed using Simon's two stage methodology with 80% power when the true response rate is 70% (Cohort 1) and 55% (Cohort 2) with an overall type I error of 5%. In the first stage of cohort 1, 15 pts will be enrolled and if there are eight or fewer clinical responses (RECIST 1.1 objective response [CR or PR] within 25 weeks of the first dose of SCIB1), further recruitment to this cohort will be stopped. The null hypothesis will be rejected if 27 or more responses are observed in 43 pts.

Results: 14 pts received the combination of SCIB1 with nivolumab and ipilimumab. 71% were male, 88% had ECOG PS 0, all had prior surgery and 24% had previous adjuvant treatment. At study entry, all patients were stage IV. The LDH was elevated in 18% and 47% had tumours with Braf mutations. 6 patients had reached the first imaging timepoint, and the objective response rate in cohort 1 is 83% . Most of the SCIB1-related adverse events were Grade 1/2. Only 1 pt reported a Grade 3 rash. No enhancement of immune-mediated adverse events were observed with the addition of SCIB1 to nivolumab with ipilimumab. Cohort 2 is ongoing.

Conclusions: SCIB1 in combination with nivolumab and ipilimumab as first line treatment for unresectable melanoma improved the ORR to 83% without an increase in clinically meaningful adverse events. These results provide confidence in initiating a randomised registration programme in unresectable melanoma pts with our novel DNA plasmid technology.

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